finally, that they "perhaps" produce or reproduce the septic poison, the possibility of their doing so, not being excluded by the isolation experiments.

In his experiments regarding putrefaction, Hiller found that a number of eggs, into some of which he injected, with proper precautions, fluid with bacteria isolated from putrefying substances, and into others, fluid with bacteria cultivated for the purpose—fifteen drops being injected—remained fresh after 10-14 days, but putrefied rapidly when air was admitted. He concludes, with Billroth, that bacteria are in themselves incapable of decomposing albumen by assimilation. He believes that in atmospheric dust, besides bacteria and other living germs, there must be other dead, corporeal, and organic matter, which constitutes the ferment of putrefaction, which might be either a ferment formed from cells or protein substances in the act of decomposing, as Liebig imagined. He proves this by the following experiment: He poured boiling distilled water on dust collected in his room, and allowed hen's eggs to soak in it, and added it to a solution fit for the development of bacteria, but which contained none. Of the four soaked eggs, only two putrefied, one quickly, and one slowly; whilst bacteria isolated from the abundant development which took place in the solution, were injected into eggs without producing putrefaction. From the fact that the dust-infusion itself after several days showed signs of putrefaction, with development of bacteria, vibrios, and afterwards infusoria, Hiller concludes that atmospheric dust must, in fact, contain putrefiable substances. —*Edin. Med. Journ.*, Jan. 1876, from *Centralblatt*, No. 49, 1875, and *Langenbeck's Archiv*, xviii.

3. *The Transferrence of Matters from Mother to Fœtus.*—At the recent meeting of the Association of German Naturalists and Physicians (*Allgemeine Wiener Medizin. Zeitung*, No. 40, 1875), Dr. Benicke described the results of some experiments which he had made by administering to twenty-five pregnant women salicyl in doses of half a drachm shortly before labour. The newly born children and the mothers were catheterized, and the urine examined for salicyl. The results were the following: 1. The interchange between mother and fœtus was very rapid. The salicyl was always given as soon as labour-pains began. In two cases, where the birth took place at the end of ten and fifteen minutes, no salicyl was found in the children. In two other cases, where the children were born forty and eighty-five minutes after the commencement of labour, no salicyl was found at first, but it was present in the urine examined some hours afterwards. In all the other cases, salicyl was found in the children's urine immediately after birth; in these cases, the shortest duration of labour was two hours. Thus salicyl had passed into the organism of the fœtus in forty minutes, and had appeared in the urine in two hours. 2. The tissue-change in the child was more active immediately after birth than in the uterus. This was shown by the stronger evidence of salicyl in the urine obtained a few hours after birth than in that removed immediately after birth. 3. Salicyl ceased to be found in the mother's urine at the end of twenty-four to thirty-six hours; in the child's urine, it was found up to the third or fourth day. The liquor amnii was obtained in a pure state in four of the cases, and was found to contain no salicyl; nor was salicyl found in the liquor amnii of several women to whom it was given for six to fifteen days before labour, although it was detected in the urine of the children.—*Brit. Med. Journ.*, Dec. 25, 1875.

MATERIA MEDICA, GENERAL THERAPEUTICS, AND PHARMACY.

4. *Transfusion of Blood.*—The No. of the *Anali Universali di Medicina e Chirurgia* for Nov. 1875, contains the concluding part of an interesting article on this measure by Dr. De Christophoris. Under the head of "Special Indicasions for Transfusion," he presents not only those resulting directly from loss of

blood, but numerous diseased conditions requiring an immediate supporting treatment. Thus we have not only Acute Anemia from hemorrhage; but chronic or slow (*lente*) anemia; chlorosis; typhus fever; puerperal fever; scurvy; scrofula; leucocythæmia; diabetes mellitus; blood poisoning; marsh cachexia; cholera morbus; eclampsia; hysterical paralysis; insanity; hydrophobia; chronic visceral diseases, as phthisis, cancer, ulceration of the stomach, and tabes dorsalis.

The cases reported are as follows: 1st. A country woman, 30 years old, affected with *physical prostration and chronic anemia*, the effect of child-bearings and nursing—great depression of forces, stomach feeble, etc. 1st transfusion resulted in restoration of force. 2d transfusion, continued amelioration; blood used, pure venous; appetite good; pulse 84. 34 days later was seized with intestinal catarrh and died.

2d. Chlorosis.—Girl 16, chalybeate treatment inefficacious; water-cure and nutritive diet failed. Five transfusions with defibrinated blood in 46 days; progressive amelioration; complete cure; two years later had no return.

3d. Hydræmia from metrorrhagia.—Peasant woman, 30 years old, with fibrous tumour of anterior and left lateral parietes of the uterus, incapable of working, subject to fainting; three transfusions with defibrinated human blood, on June 27th, July 2th, and 20th, 1868; cure complete, and no return.

4th. Marsh cachexia.—Peasant, 40 years old. Two transfusions with non-defibrinated human blood; attack of suppurative villous pericarditis, "not a rare condition in this disease," and death.

5th. Splenic leucocythæmia.—Child 3 years old; spleen much enlarged; stomach very weak; prostration extreme; one transfusion of defibrinated blood, slight signs of improvement for a day, then increase of prostration, and death.

6th. Chlorosis.—Woman 26. Two transfusions of defibrinated blood 18 days apart. After first trial respiration fell gradually in twelve days, from 48 to 24, and appetite at once increased, so that in seven days it became almost insatiable. The menses, which had been suspended for two years, returned after first transfusion, and again in 32 days; one year later, menses regular, health good, complexion florid.

7th. Leucocythæmia, in a girl of 18, affected by a return of miasmatic fever. Two transfusions in 22 days; catamenia appeared after second, cure.

8th. Epilepsy.—Girl of 20; convulsions every day, probable cause chlorosis; transfusion; no fit for eleven days; attack of profuse diarrhœa from drinking abundantly of cold milk, with return of convulsions; passed from observation; cure uncertain.

9th. Hysteria.—Spinal irritation with vomiting of long standing, resisting all forms of treatment; transfusion with defibrinated blood; cessation of vomiting; restoration to health.

Much attention has been paid in Germany to the value of transfusion of blood in disease; and the question has been taken up with great interest in Italy: with us it has had but little attention paid to it, except as a restorative after profuse hemorrhage. R. P. H.

5. *Surgical Anæsthesia in Children by Chloral administered by the mouth.*—Prof. Bouchut publishes in the *Bulletin de Thérapeutique* (Oct. 30th) an abstract of a communication which he made to the International Congress at Brussels. Without discussing the relative merits of the various anæsthetic procedures which the surgeon may resort to, he wished to make known to the Congress that in children absolute anæsthesia may be obtained by administering chloral by the mouth. This action of the drug is certain and easy of production, and cannot be obtained in the adult—furnishing an additional proof of the difference in the action of certain medicinal substances in children and adults. Whether it is that the adult cannot swallow without disgust or intolerance a sufficient quantity of chloral, certain it is that he cannot be anæsthetised by it, for it would be necessary to raise the dose to eight or ten grammes, and this is a dose which the stomach either refuses or rejects. In the child, on the other hand, three or four grammes are taken without any difficulty, this producing neither pyrosis, gastritis, vomiting, nor diarrhœa, while it gives rise to a more

or less intense anæsthesia. Prof. Bouchut is enabled to found this statement upon a considerable number of facts, having made very frequent trials of the hypnotic and anæsthetic powers of chloral ever since it was first imported into France, in 1869, by Demarquay, who denied that it produced any anæsthetic effect. Prof. Bouchut has often employed it at the Hôpital des Enfants Malades, in chorea, in cerebral rheumatism, or during the opening of abscesses and the extraction of teeth. He has been in the habit of prescribing three or four grammes for from ten to twelve children daily, sometimes continuing it for three weeks, a month, or longer—so that he can refer to something like from 8000 to 10,000 cases of its employment, and amidst this immense number he has never met with a fatal accident. In one case only did asystolia seem imminent, in a child suffering from mitral insufficiency. In several instances chloralic eruptions have followed, but these have been of no consequence, only lasting for a few hours. Intestinal irritation has never been produced, even when the chloral, in doses of from three to six grammes, has been continued for a month or six weeks, so that the same child has taken in that time from 200 to 240 grammes of the medicine. Prof. Bouchut, who was the first to use chloral for chorea in 1869, has had cases which, from their violence, seemed to threaten death, and have been cured by chloral given in three-gramme doses, morning and evening, for fifteen or twenty days. It is the best remedy we have for this disease, and is, indeed, absolutely necessary when the movements are so violent as to excoriate the skin and cause death. By forcing upon the patient sixteen or eighteen hours of sleep and immobility out of the twenty-four hours, the skin ceases to suffer, the movements diminish, and the chorea is cured. The same effects of chloral may be produced by chloral suppositories, prepared according to M. Mayet's formula (*Bull. de Thérap.*, t. 88, p. 318); but the rectum is more irritable than the stomach, so that after three or four days the chloral suppositories induce tenesmus and rectal heat and ardor, which compel their discontinuance. The stomach is the best channel of administration of chloral for children, as by it the remedy is easily given, and its tolerance is complete. A quarter of an hour after its ingestion the anæsthesia commences, and at the end of the hour it is complete; and if now an abscess is opened or an incision made, the sleeping infant heaves a sigh, or sometimes moves a limb, without awakening, and again becomes immovable, being quite unaware of what has passed on awakening for four hours afterwards. The same occurs in the destruction of erectile tumours by the Vienna paste, or the extraction of teeth. At the Hôpital des Enfants Malades the sister gives a dose of three or four grammes of chloral at eight o'clock, the child falling asleep in twenty minutes, and at nine the dentist arrives and removes one or even two teeth without awakening the child. By those who know the pain and difficulty of removing teeth in children, the valuable character of this chloral anæsthetic will be appreciated.—*Med. Times and Gazette*, Dec. 11, 1875.

6. *Jaborandi.*—Dr. WM. CRAIG, Lecturer on Materia Medica, Edinburgh School of Medicine, has instituted a number of experiments with this drug, some of which fully confirm what is already known regarding its sialagogue and diaphoretic powers, and has added some points to our previous knowledge.

Dr. C. injected up the rectum the infusion prepared from one drachm of the bruised leaves, and found that salivation and perspiration came on as speedily and as effectually as when the same quantity was administered by the mouth, clearly proving that the active principle of jaborandi is first absorbed, and afterwards produces its remarkable physiological effects.

With regard to the active principle of the drug Dr. C. says: "Various chemists have analyzed the leaves, and it is generally believed that its activity is due to an alkaloid, which some have called pilocarpin. The watery infusion of jaborandi is acid, but whatever be the acid contained in jaborandi, its physiological properties are not due to this acid. Neither are they due to the volatile oil contained in the leaves, and to which they owe their characteristic odour. For I have had prepared for me by J. F. Macfarlan & Co. of this city, a substance called pilocarpin, which undoubtedly possesses the physiological properties of the drug, and yet is not acid, and does not contain the characteristic odour of jaborandi. It is quite possible, for anything I know, that the acid and volatile oil may possess sialagogue or diaphoretic properties, for I am not aware that they have as yet been isolated; but it is clearly proved that there is a substance which can be separated from jaborandi, destitute of acidity and of the characteristic odour of that plant, and which possesses all the activity of the drug. This substance, called *pilocarpin*, is of a semi-fluid consistence, of a yellowish colour, and possessed of an agreeable odour. It is soluble in water, and is very active. One grain of this pilocarpin is nearly as active as one drachm of the leaves. Whatever be the active principle of jaborandi, it is something which is soluble in water, and even the *strained* infusion possesses all the activity of the drug. In this opinion, I differ from others who have experimented with this substance. There are many who believe that to produce the physiological effects of jaborandi, it is necessary to use either an alcoholic preparation, or to swallow the 'dregs.'"

Dr. C. considers this view to be erroneous. The whole of his experiments, he says, "have been performed with the strained infusion, and this substance called pilocarpin, which I have found to be so active in doses of one grain. It is freely soluble in water. These facts clearly prove that the active principle of jaborandi is soluble in water, and also that the strained infusion possesses all the activity of the drug.

"Regarding the effects of this medicine on the temperature, pulse, and vision, experimenters are somewhat divided. My own experience leads me to believe that they are very small and insignificant. I have never found jaborandi affect much either the heart's action or the temperature of the body, and I have watched carefully for the disturbance of vision observed by Mr. Martindale and others, but as yet have failed to observe it. I believe that many of the untoward results ascribed to jaborandi are due to the fact that 'dregs' have been swallowed in addition to the strained infusion.

"I have not had much opportunity of testing the therapeutic virtues of this drug, but I have tried it in several cases of fever, where the tongue was dry and the mouth parched, and by giving small doses of the infusion every few hours, I was enabled to restore the flow of saliva, and to keep the tongue and mouth moist. I believe that in this respect it will prove of considerable benefit in fevers and allied diseases. It has also been efficacious in removing pleuritic effusions. For this disease it will yet prove a most valuable medicine; for in a few hours, in addition to profuse perspiration, twelve or sixteen ounces of fluid may be withdrawn from the blood, with very little disturbance to the general system, which must tend in no small degree to promote absorption of fluid from the pleural cavities. I understand it has been found useful in diabetes. Several cases of this disease have been successfully treated with jaborandi by Professor Laycock.

"Regarding the applications of jaborandi to the cure of disease, much clinical observation is still necessary before we can assert positively what are the therapeutic virtues of this remarkable drug.

"The following may be regarded as well-ascertained facts regarding jaborandi:—

"1. Its leaves are possessed of remarkable sialagogue and diaphoretic properties.

"2. Boiling water is capable of extracting the most, if not the whole, of these properties.

"3. A strained infusion seldom produces any untoward results.

"4. On account of the large quantity of indigestible fibrous materials in the 'dregs,' these, when swallowed, must produce unpleasant effects.

"5. A substance of a semi-fluid consistence, destitute of acidity and the characteristic odour of jaborandi, may be separated, possessing all the activity of the drug, and which is probably an alkaloid.

"6. The dose will be found to be $\frac{1}{12}$ to $\frac{1}{4}$ grain of this alkaloid, and of the infusion as much as corresponds to five or ten grains of the leaves."—*Edinburgh Med. Journ.*, Jan. 1876.

7. *Therapeutic Action of Coto Bark.*—Prof. VON GIETL writes on this subject in the *Archiv für Pharmacie*, September, 1875 (abstract in *Allgemeine Medicin. Central-Zeitung*, November 20th): Coto bark is obtained from a tree in the interior of Bolivia. It is there used in the form of powder or of alcoholic extract in cases of diarrhœa, colic, and neuralgic toothache; also in tincture in rheumatism and gout. The description of it apparently indicates that it does not belong to the cinchona class (though growing in the district where these trees flourish), but that it is probably one of the *Lauraceæ* or *Terebinthinaceæ*. Wittstein finds its chief constituents to be, an ethereal oil; a fluid alkaloid, having a smell of herrings and urine, and thus resembling propylamin and trimethylamin; and hard and soft woody matter. It also contains starch, gum, sugar, oxalic acid, tannic acid, etc. Sixteen patients were treated with it—fifteen males and one female. It was given sometimes in fine powder, sometimes in the form of tincture made with one part of coarsely powdered bark and nine parts of spirit of 85 per cent. The powder was given in eight cases, the tincture in seven; both together in one case. The dose of the powder was 7½ grains four or six times daily; of the tincture, 10 drops every two hours. The cases in which it was given were, two of diarrhœa in pulmonary phthisis; five of diarrhœa from cold and hospital diarrhœa; six of non-febrile gastro-intestinal catarrh with diarrhœa; three of febrile gastro-intestinal catarrh with violent diarrhœa. The powder and tincture were given together in one case of diarrhœa with phthisis. In one case only, neither the powder nor the tincture could be continued, as both produced severe burning pain in the abdomen and vomiting; the patient was phthisical. In another phthisical case, the powder produced much distress, while the tincture was easily borne. Dr. von Gietl believes that the coto bark is a remedy of very great value in the various forms of diarrhœa.—*Brit. Med. Journ.*, Dec. 25, 1875.

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8. *Action of Croton-Chloral-Hydrate.*—Dr. N. JERUSALIMSKY has made a series of experiments with croton-chloral-hydrate, the results of which show that this agent possesses the power of diminishing the pressure of the blood, and that the diminution occurs both with the cerebral centres uninjured, and after their action has been abolished; it therefore exerts a paralyzing action on the heart. When small doses were administered the respiratory activity was retarded; with larger the respiration was arrested. Much larger doses are required to produce sleep than in the case of chloral; control experiments showed that it possesses no specific influence on the fifth or any other sensory nerve. No sleep was obtained by the administration of forty grains in a case of prosopalgia, though it produced malaise, tightness of the chest with feeling of exhaustion, and a pulse of 120. On making the patient breathe oxygen the number of pulsations fell considerably. In a second case in which it was given a neuralgic affection from which the patient suffered was cured, and in a third the pain was alleviated.—*Practitioner*, Jan. 1876, from *Mosk. Med. Zeitung*, No. 17, 1875.

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9. *The Physiological Action of Alcohol.*—The Nos. of the *Practitioner* for January and February of the present year contain an instructive paper on this subject by Dr. T. LAUDER BRUNTON. The direct points in this paper are summed up as follows:—

1. Alcohol, in small quantities, increases the secretion of gastric juice and the movements of the stomach, and thus aids digestion. Although unnecessary in health, it is useful in exhaustion and debility.

2. It increases the force and frequency of the pulse, by acting reflexly through the nerves of the stomach.

3. In large doses it impairs digestion by over-irritating the stomach.

4. It may produce death reflexly by shock.

5. After absorption into the blood, it lessens the oxidizing power of the red blood corpuscles. This property renders it useful in reducing temperature; when constantly or very frequently present in the blood, it causes accumulation of fat, and fatty degeneration of organs.

6. It undergoes combustion in the body, maintains or increases the body weight, and prolongs life on an insufficient diet. It is therefore entitled to be reckoned as a food.

7. If large doses are taken, part of it is excreted unchanged.

8. It dilates the bloodvessels, increases the force and frequency of the heart by its action on the nervous centres, to which it is conveyed by the blood, imparts a feeling of comfort, and facilitates bodily and mental labour. It does not give additional strength, but merely enables a man to draw upon his reserve energy. It may thus give assistance in a single effort, but not in prolonged exertions.

9. The same is the case with the heart; but in disease alcohol frequently slows instead of quickening the pulsations of this organ, and thus economizes instead of expending its reserve energy.

10. By dilating the vessels of the skin, alcohol warms the surface at the expense of the internal organs. It is thus injurious when taken during exposure to cold, but beneficial when taken after the exposure is over, as it tends to prevent congestion of internal organs.

11. The symptoms of intoxication are due to paralysis of the nervous system; the cerebrum and cerebellum being first affected, then the cord, and lastly the medulla oblongata. It is through paralysis of the medulla that alcohol usually causes death.

12. The apparent immunity which drunken men enjoy from the usual effects of serious accidents, is due to paralysis of the nervous mechanism, through which shock would be produced in a sober condition.—*Practitioner*, Feb. 1876.

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10. *Researches on the Physiological Properties of Aconite and Aconitina.*—M. Guillaud in a thesis on this subject asks, Does aconite, or rather the *Aconitum napellus*, owe *all* its properties to the aconitina that it contains, and can the latter be substituted for it? Schroff, and more recently M. Gubler, have sought to establish a distinction in stating that aconitina was only a narcotic, whilst aconite was both a narcotic and an acrid. M. Guillaud, however, believes from an examination of all that has been recorded of them, that their action is identical, and may be summed up in these words: that they are capable of producing disturbance of the alimentary canal, of the motility of vision, of respiration, and of the circulation, with conservation of the functions of the brain till death takes place, as it ultimately does, by asphyxia or syncope. Three opinions have been expressed in regard to the action of aconitina. (1) By Holtot and Liégeoris, and more recently by Bœhm and Wartmann, it is a poison that paralyzes the central nervous system. (2) By Aschscharumow and Gréhant it is believed to be a poison paralyzing the peripheric motor system. (3) Lastly, by M. Leven, it is held to be a poison attacking simultaneously the central nervous system and the muscular system, and paralyzing both. In view of these discrepancies, M. Guillaud took up the subject. His experiments were made on various classes both of the vertebrata and of the invertebrata in the physiological laboratory of Montpellier, and the poison was injected subcutaneously in solution in water, with the addition of a few drops of acetic acid. Many of his experiments gave results in opposition to those of previous experimenters. Thus, M. Leven stated that an animal poisoned with aconitina died without convulsions tranquilly as in death by veratria and digitaline. This is an error. Convulsions are never absent during the first period of poisoning in healthy animals not anæmic from fasting, and even when the convulsions have ceased the muscles long remain irritable to induced currents, which is in direct opposition to aconitina being a muscular poison; on the other hand, M. Gréhant considers that aconitina first paralyzes the motor nerves; and that when given in small doses it acts like woorara. This is also the opinion of Aschscharumow. M. Guillaud considers that this is not a correct view, and these are the facts he regards as being in opposition to it. In addition to the circumstance that the paralysis of the motor nerves is only secondary, and that it only occurs like central paralysis after a period of hyperæsthesia, it is, which is very important to note, always consecutive to this last paralysis. At first,

when an animal is poisoned, the slightest touch, any sound, is sufficient to agitate it strongly. The sensibility then gradually becomes more and more obtuse, and when pinching of the skin or even irritation of the spinal cord no longer produces any effect, an induced current applied over the course of a motor nerve still causes the muscle to contract for some time; the excitability of the nerve appears in fact to die out from the centre to the periphery. If one of the posterior members of the leg of a frog be preserved from the action of the poison by a ligature, contractions occur in the ligatured leg as intense in degree as in the opposite one; and the contractions that ensue on pinching the skin are also equally energetic on both sides—a sufficient proof that, in the first instance, aconitina acts neither on the motor nerves nor on the muscles; at a later period the motor nerves and muscles become successively affected, and the foot preserved alone remains excitable. M. Guillaud's observations of the action of aconitina on the heart are again not conformable to the results obtained by Aschscharumow and Gréhant. These observers find that aconitina in the large dose (for a frog) of a milligramme, first stops the action of the heart, even before it has been able to distribute the poison to the system, and the motor nerves are then not poisoned because they have scarcely received any of the poison. But according to M. Guillaud the heart, whether the dose be large or small, first shows the effect of the poison by beating rapidly, then more slowly, some seconds intervening between the beats; but it does stop till reflex movements have ceased, this of course taking place earlier with stronger doses. The hearts of frogs excited and placed in solution of aconitina seem to be acted on slowly, continuing to beat sometimes for ten minutes, as long in fact as a heart placed in a saline solution. M. Guillaud describes a series of phenomena during the earlier stages of the action of aconitina, viz., disturbances of locomotion, disordered movements, rapid and interrupted respiration, salivation, excessive secretions—all phenomena indicating hyperæsthesia of the nervous centres. The hypersecretions may be regarded as analogous phenomena to the exaggerated muscular contractions, since Rouget has demonstrated the existence of secretory nerves passing to the poison glands of the dorsal natatory membrane of the larvæ of the salamander. The author, resuming his researches, distinguishes three periods in aconite poisoning—a period of contraction, a period of deliquium (*resolution*), and a period of muscular death. Aconitina acts essentially on the centres of the spinal cord and medulla oblongata by first augmenting these excito-motor functions like strychnia and the salts of silver. It then gradually paralyzes them. In regard to the encephalon, the centres of voluntary movements are attacked and much enfeebled, whilst the sensory centres remain, in part at least, uninjured. Aconitina, then, paralyzes successively the sensory nerves, the motor nerves, the sympathetic nerves, and then the muscles. Variations in the dose cause no alteration in the order of these symptoms. It affects the respiration through the medulla oblongata, and not otherwise, and by this action causes death in the higher animals. So also aconitina only acts on the heart, eye, and pupil, through the intervention of the nervous system. Its essential action is, in fact, as Hottot and Liégeois originally maintained.—*The Practitioner*, Dec. 1875, from *Archives du Physiologie*, Aug. and Sept. 1875.

11. *The Action of Chloral-Hydrate and Croton-Chloral-Hydrate.*—J. V. Mering (*Archiv für Experimental Pathologie und Pharmak.*, iii. 185, and *Centralblatt*, No. 37, 1875) states from his experiments, that croton-chloral-hydrate, when given in small doses to rabbits before the cessation of the reflex action from the cornea, considerably retards the respiration; and when the corneal reflex action is extinguished, the number of respirations is diminished by a half. The substance (0.6 gramme) was introduced subcutaneously, or divided in scarcely half as large total doses and injected into the veins. Similar results were obtained with parallel experiments with chloral-hydrate. Croton-chloral-hydrate acts upon the frog's heart similarly to chloral-hydrate, even small doses (0.025 gramme given subcutaneously) causing cessation of its action. Blood-pressure experiments upon dogs, cats, and rabbits were performed with both substances. Small doses diminish the blood-pressure temporarily, and

large doses diminish it continuously, till the blood-pressure curve reaches the abscissa. The pulse-beats are at first increased by both drugs, and this increase lasts somewhat longer with croton-chloral-hydrate. At a certain stage of the experiments the blood-pressure remained continually low, in spite of great blood-movements. This seems to show that the croton-chloral-hydrate extinguishes the arterial tonus, the heart's energy still continuing; this being, as is known, asserted of chloroform and chloral-hydrate. From these and former experiments, there seems to be a great similarity in the actions of the three above-mentioned drugs.

Lastly, the author combats Liebreich's theory of the action of croton-chloral-hydrate. According to this theory this substance in alkaline blood splits up into dichlorallylen, hydrochloric acid, and formic acid, and the former, analogous to aethyliden chloride, is the active factor.

The author employed only the trichlor-crotonate of soda, which even in the cold in dilute alkaline solutions passes into dichlorallylen. This substance was injected into rabbits, and, even when five grammes were injected, it had no effect.—*London Med. Record*, Dec. 15, 1875.

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12. *Chloral as an External Application.*—Dr. Wm. Craig, Lecturer on Materia Medica, Edinburgh School of Medicine, states (*Edin. Med. Journ.*, Feb. 1876) that he has tried extensively a lotion of 5 to 15 grains of chloral to the ounce of water and found it an excellent dressing to ulcers and wounds. He says further: "I also used chloral solution as an injection into the sacs of large abscesses, and found that it tended much to diminish secretion and make the parts heal. I found it also a useful lotion for the eye in inflammatory conditions of that organ. It is an excellent application to burns, and very specially where there is a fetid discharge. I also found it a good application to remove warts from the hands and fingers. I used for this purpose a lotion containing 15 to 20 grains to the ounce of water, applied by means of lint and gutta-percha. It causes no pain, and the wart speedily becomes smaller, and gradually disappears.

"I also used it as a lotion to sore nipples and to inflamed mucous membranes. When chloral is applied to an ulcer, a wound, or to the interior of an abscess sac, it causes at first some smarting, but that only lasts for a few minutes, and is soon succeeded by a most agreeable sensation. Patients so treated have frequently told me that soon after the lotion was applied a very agreeable soothing effect was felt in the wound. I believe that in all such cases chloral acts as a local sedative. It produces anæsthesia of the nerves of the part. Wherever there is a wound or ulcer there is irritability of the nerves of that part; and chloral, by soothing this irritability of the nerves, favours the healing process.

"I have frequently used with good effect an ointment containing 30 to 60 grains of the hydrate of chloral to the ounce in eczema and other allied affections. I believe it to be one of the best applications in such diseases: and a medical practitioner lately told me that he had used it with marked benefit as a local application during an attack of erysipelas of the head."

Dr. P. H. Watson, who has extensively used chloral in various forms, writes to Dr. Craig: "I have in my wards made use of the chloral hydrate for fully six months, and find it quite as active as an antiseptic as carbolic acid or boracic acid. It approaches nearer to carbolic acid in its effects than to the boracic acid, especially in that it is volatile, and thus by its vapour penetrates and surrounds parts to which as a dressing it has been applied with an atmosphere of itself.

"It has a marked advantage over carbolic acid, in so far that its odour is pleasant, resembling some of the ethereal compounds employed for flavouring purposes. It also is absorbed, and, in being so, deadens pain after an operation."

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13. *Butyl-chloral.*—In a recent article in the *Deutsche Medizinische Wochenschrift*, Dr. Oscar Liebreich states that Messrs. Krämer and Pinner, in the course of their researches on the substance commonly called croton-chloral, have ascertained that it contains two more atoms of hydrogen than was sup-

posed, and that it is in fact butyl-chloral. When soda or another alkali is mixed with it, it undergoes decomposition, chloride of sodium, formiate of soda, and bichlorallylene being produced.

$$C_4H_5Cl_3O+NaO=NaCl+CHNaO_2+H_2O+C_3H_4Cl_2.$$

The physiological action of butyl-chloral is, Dr. Liebreich has ascertained from a large number of experiments, very constant. In rabbits anæsthesia is always found to commence at the head, a state of hypnotism having been already produced. The animals, while sitting quietly, let the head drop; and anæsthesia of this part now appears, while reflex action can be excited in the limbs; from the head, the anæsthesia spreads over the body, and reflex action is not caused by irritation. The respiration and pulse become slow; and, with a fatal dose, the respiration ceases before the pulse. The *post-mortem* appearances differ from those of poisoning by chloral, in that in the latter paralysis of the heart is found, both ventricles being full of blood; while in death from butyl-chloral the left ventricle is contracted and nearly empty, the right cavities and the lungs being charged with blood. With this difference in the *post-mortem* appearance corresponds the difference in the mode of death; in chloral-narcosis general anæsthesia is rapidly produced; *i. e.*, the action of a large dose passes quickly from the cerebrum to the medulla oblongata, and the heart's action ceases while the respiratory movements continue.

In chloral-poisoning, Dr. Liebreich says that artificial respiration is useless; the heart's action can only be restored by the action of strychnia on the cardiac ganglia. With butyl-chloral, on the other hand, the heart's action can be re-excited by artificial respiration. This may be seen in an animal whose thorax has been opened during the narcosis.

Chloral, then causes death by interfering with the cardiac ganglia; butyl-chloral, by its action on the respiratory centre. And just as the ganglion-cells of the heart are stimulated by strychnia, so continued artificial respiration overcomes the narcosis of the medulla oblongata.

Dr. Liebreich points out as a fact of practical importance, that the duration of the stages in the narcosis produced by butyl-chloral is about two-thirds less than in that produced by chloral.

In man as in animals, anæsthesia commences at the head, while reflex action can still be excited on the limbs. Some experiments on a child, detailed by Dr. Liebreich, show that even in the waking state there is anæsthesia of the cornea while the nasal mucous membrane is still irritable. With a dose of chloral sufficient to produce anæsthesia of the eye, there would also be general anæsthesia of the whole body.

Doses of butyl-chloral sufficient merely to produce anæsthesia of the head do not essentially affect the pulse and respiration. In insane adults, Dr. Liebreich has found doses up to 5 *grammes* to produce sleep and anæsthesia of the head, with maintenance of the muscular tonus and of reflex action in the trunk, so that the patients remained sitting while the head was perfectly anæsthetic.

Though as yet unable to adduce any practical experience on the subject, Dr. Liebreich believes that butyl-chloral may be very useful as an anæsthetic in operations on the head, especially when, as is sometimes the case, it is impossible to give anæsthetics by inhalation.

The practical value of butyl-chloral, Dr. Liebreich says, lies in its property of diminishing sensibility before producing narcosis. He entertained the hope at first that it would be useful in tic-douloureux; but in the cases in which he has given it, he has, he says, certainly observed relief of the pain, but not an arrest or cure of the malady. The action of butyl-chloral is of less duration than that of morphia; a comparison of the general effects of the two remedies indicates that butyl-chloral should be preferred to morphia or combined with it. Dr. Liebreich observed the action of butyl-chloral in a most marked manner in two cases of tic, in which the tenderness was so great that the patients could not bear to touch the painful parts of the face or to bring a handkerchief near their noses. A *gramme* of butyl-chloral produced complete relief, lasting generally for two hours, each time that the dose was repeated.

Regarding the mode of administration of butyl-chloral, Dr. Liebreich says that at first he tried an alcoholic solution; but he has found that, after long standing, some change takes place which greatly impairs the action of the butyl-chloral. He now orders it in the following form: butyl-chloral-hydrate, 5 to 10 parts; glycerine, 20; distilled water, 130 parts. The mixture requires to be shaken before being used. The dose is half an ounce, followed in five minutes by a second, and in ten minutes by a third. It is well to begin with a small dose, so as to avoid producing hypnotism— that is, where the anæsthetic effect alone is desired. To produce sleep, one, two, or three *grammes* (15 to 45 grains), according to the patient's constitution, are to be given at bedtime.

Butyl-chloral gives relief in painful affections of the teeth; but of course a radical cure can only be effected by attacking the cause of the disease. It should, whenever possible, be taken after meals, and be followed by a copious draught of water.

Whether any advantage is to be derived from combining butyl-chloral with ordinary chloral or with alkaloids, must be decided by further experiments.—*Brit. Med. Journ.*, Feb. 12, 1876.

14. *Action of Nerve Sedatives.*—The *British Med. Journal*, for Jan. 1, 1876, contains some instructive remarks on our chief nerve sedatives.

"The first of these is opium, which seems first to rouse action in the nervous system and then to arrest it. It is well known that by practice and continual consumption of this agent its first action can be prolonged in a surprising manner, as in the cases of confirmed opium-eaters; but there are long reactions of nervous exaustion and of lethargy after such manifestations. Here we are rather concerned with the action of opium as a medicine, and administered to persons not habituated to its use; the effect of habit being the same with opium as with alcohol. The amount of alcohol which a well-seasoned toper will imbibe with the consequence of gentle exhilaration, would produce profound comatose sleep in one not habited to its use. . . . .

"The effect of a moderate dose of opium upon an ordinary person is to produce sleep. There is first a period of gentle stimulation with cerebral activity, and then follows a sound, but not necessarily dreamless, sleep. If the dose be increased, there results a death-like coma, with great depression of the circulation and slow irregular respiratory movements. If the dose be fatal, 'death occurs generally by failure of the respiration and almost complete extinguishment of the vital functions' (Wood). Thus we see that the higher faculties associated with the cerebral convolutions are first affected, and then ultimately the action of the centres at the base of the brain is abolished. Consequently, we find that voluntary motion disappears while the movements of respiration and the circulation are but little affected; but that a larger dose will entail arrest of action in the movements so essential to life.

"Opium, however, does not act merely upon the cerebro-spinal system; it acts equally upon every nerve-cell, and also probably upon every nerve-fibre. Gschiedlen found that morphia acted upon the respiratory centres as well as upon the intracardiac motor ganglia. Opium, too, acts upon the centres in the cord associated with the bladder, and under its influence the calls to empty it are less felt and are less imperative. In a similar manner, opium acts upon the local ganglia in connection with the intestinal canal arresting peristaltic action as well as the intestinal secretion. Consequently, we find that, while we can arrest diarrhœa by the use of opium, its administration for other ends and purposes entails constipation and loss of appetite. That is, by its effects upon the local centres, intestinal movement and secretion are arrested, hence constipation; and by the same action the sensations of hunger are less distinctly felt, less perfectly manifested. In colic, in bulimia, in simple diarrhœa, opium is indicated; as well as in peritonitis, where, by arresting the peristaltic action, it gives relief and limits suffering.

"In this latter action, however, its other effects come into play, viz., its effects upon sensation. Not only does opium act beneficially in peritonitis by arresting peristaltic movement, and consequently limiting the friction upon each other of inflamed serous surfaces, but it deadens the receptivity of the sensory centres and obviates the consequences of painful sensations. This part of the action of opium deservedly attracts our attention. Let us take some simple form of pain; for instance, onychia of the great toe. A dose of opium lessens the pain; a larger dose brings about a condition where the pain is no longer felt, but still sleep is not produced; a still larger dose, and sleep ensues. On analyzing this action, we find that opium does not act solely upon the encephalic portion of the nervous system, but upon each nerve-cell and each nerve-fibre, in all probability; and that its action is in some such way antagonistic to that of pain. Pain, if intense, does not admit of sleep; but if, after several days and nights of wakefulness brought about by pain, as in a whitlow, for instance, local relief of suffering ensue, then sound dreamless sleep quickly follows. The exhaustion of the nerve-centres from their long wakefulness is followed by long lethargy, as soon as the perturbations produced by painful sensations no longer pass in from the periphery. An analgesic is an agent which lessens pain; and that opium is *par excellence.* It would seem that opium not only lessens cerebral receptivity, but that it also deadens nerve-conductivity. In small doses, it but palliates pain; in large doses, it more perfectly neutralizes painful sensations, and this may be achieved without the condition of cerebral inactivity—sleep—being induced; by a still larger dose, sleep is brought on. In the absence of direct experiment, we are shut up to the results to be obtained by close clinical observation. These lead us to the conclusion that the action of opium is antagonistic to the effects of pain, and that it relieves pain, not only, in all probability, by its effects upon the encephalic centres, but by its effect upon each nerve-fibril along which the pain-producing impression travels, and upon every nerve-cell through which this impression passes. The consequence is, that the impression transmitted from the periphery is diminished as it travels, until, when received in the brain, it is reduced below a pain-producing point; the effect of opium on the cerebral centres being a factor in the production of this result. Consequently, when opium is given in peritonitis, it neutralizes the resultant effects of the friction of two inflamed surfaces, and relieves the system from the consequences of intense pain.

"That opium does so act, is further rendered probable by its effects upon terminal nerve-fibres. Thus, we apply it locally to bruises, to painful ulcers, to inflamed joints, to piles, etc. We utilize its local action in the use of morphia suppositories, in hypodermic injections into painful parts, where we wish to secure local action as well as systemic effects. This carries us a step further. It renders it probable that in peritonitis opium lessens the first impressions of pain by its effect upon the nerve-fibrils in the peritoneum. Not only so, but Brunton found that opium exercised a very decided effect in limiting vascular congestion in a part where he was artificially exciting inflammation. He was led to suppose that a part of the good effects of opium in inflammations is due to this limitation of the blood-supply, just as lifting the hand above the head relieves an inflamed finger. This local effect upon the vascular supply, together with the effects of opium upon the nervous system, goes far to explain its use in serous inflammations.

"Taking sleep to be the most pronounced physiological state of cerebral inactivity, the inquiry how it is brought about becomes highly interesting in a practical point of view. For its production, two factors are requisite. The first is an effect upon the cerebral cells, by which their activity is lessened, and a part of this is their diminished power to attract blood to themselves; the second is a condition of cerebral anæmia. It is of importance to remember these two actions, according as insomnia occurs with an active circulation, a full and bounding pulse, or with a low blood-pressure. When the arteries are full and the heart is acting vigorously, sleep will scarcely be produced except by combining opium with a cardiac depressant, as in its union with antimony in the treatment of sthenic conditions. The effect of opium upon the cerebral cells would in itself be insufficient for the end aimed at, if that action were not aided by a distinct impression upon the circulation. By limiting the blood-supply to the brain in addition, the hypnotic effect can be secured.

"On the other hand, sleep will not be brought about necessarily by producing cerebral anæmia, though loss of function follows arrest of the arterial blood-supply to the brain, as has been found by experiment; and a good meal, a seat near a warm fire after a long walk in a cold wind, will induce deep sleep in the majority of persons, no matter how lightly they ordinarily slumber. Here the blood-supply to the brain is so diminished that loss of functional activity follows. In the same way, in simple conditions of cerebral activity, an agent producing cerebral anæmia conduces to sleep.

"Most hypnotics possess this double action. Thus, opium not only arrests nerve-action, but both Nothnagel and Gschiedlen have found that, after a brief period of increase in the pulse-rate and in arterial tension, a fall in each follows; and Max Schuler found the vessels of the pia mater to be first dilated, and then distinctly contracted by opium. This corresponds to the first period of stimulation observed by others. Hydrate of chloral also possesses this double action; but with it the effect upon the circulation is very pronounced as compared with opium. It is a difference in degree, however, not in kind. Chloral affects the nervous system, and possesses some power when applied locally to the peripheral ends of nerves, as well as acting upon the circulation. It is, however, found that, as an analgesic, chloral is far below opium and morphia. This we can comprehend from its more limited effect upon the nervous system. On the other hand, where sleeplessness is the result not of pain so much as of a simple inability to get off to sleep, of a condition of cerebral vascularity merely, then chloral is the remedy *par excellence*. In the high arterial tension of chronic Bright's disease, the sleeplessness which ensues is due to cerebral vascularity, and opium does not act well under those circumstances, but chloral suits surprisingly. Where sleeplessness is due to painful impressions coming in from the periphery, chloral is comparatively useless, and opium is our trustiest agent. It is of importance to recognize these distinctions in the action of these two allied agents; so that in practice they may be used, each in the case for which it is best adapted, and not substituted for each other capriciously. Of course, they may be combined in many cases with advantage. In sub-inflammatory conditions with considerable pain, such combination is especially indicated.

"In consequence of its powerful effect upon the cardiac ganglia, and its depressant effects upon the circulation, chloral must be used but cautiously in cases of cardiac debility. Da Costa urges this in his Toner lectures. Not only in cases of cardiac adynamy, but in other cases where an enlarged and correspondingly powerful ventricle is faltering before a tight stenosis, chloral is contraindicated, as it has been found under these circumstances to produce a paralyzing effect upon the heart of a most undesirable character. In cases of high arterial tension it is very useful, and forms an excellent hypnotic. Chloral is also found to diminish the activity of the uterine contractions in parturition. In some cases of convulsions or chorea, it is also useful; while it has been found of decided service in the treatment of tetanus, giving relief where cure is unattainable.

"As a pure hypnotic, chloral is, perhaps, unequalled; and, in choosing betwixt it and opium, the peculiarities of each case must be fully weighed; in some cases, their combination is indicated. It must be borne in mind, however, that the continued use of chloral is liable to induce a condition of brain-bloodlessness of an objectionable character, a loss of brain-power resulting in ordinary individuals; while under its too free use melancholia is apt to pass into the more pronounced condition of dementia.

"In bromide of potassium, we possess an agent of decided power in controlling the activity of the nervous system. It also possesses some power as a vascular depressant; but its action is very decided upon the nervous system, especially in lessening reflex action. In toxic doses, it produces loss of memory, confusion of thought, with a torpidity and a tardiness of comprehension and answer (Nothnagel). In fatal doses it brings the heart to a standstill in diastole, probably by its effects upon the cardiac ganglia, as well as the action of potash on the muscle of the heart. It is not, however, used largely when the end desired is lowering of the arterial tension, along with the allaying of nervous irritability or excitement; there chloral is more useful, or a combination of the two may be resorted to. Bromide of potassium exercises a very pronounced action upon the reproductive organs; and, in cases of orexia, or exaltation of the generative instinct, is unequalled by any other remedy we possess. Not only does it have its local effect; it has, as well, an effect upon the transmission of sensations arising in peripheral impressions, and so reduces both the local action and the cerebral effect; but it also lessens markedly the reaction of the cerebral activity upon the parts. This is well shown by the decided effects produced by its free administration in the menorrhagia of young females. In controlling convulsive seizures, it is very serviceable, and it has almost changed the aspect of epilepsy. It is, perhaps, most valuable in convulsive movement the result of far-away irritation. In the epileptic fits associated with irritation in the reproductive organs, it is of inestimable value. In other actions which are reflex, it is markedly useful. In the vomiting of pregnancy, it is now commonly resorted to. In other reflex actions connected with this condition, it is equally beneficial, as in diarrhœa for instance, or in salivation in the pregnant state. Salivation arising from distant irritation other than pregnancy is equally relieved by it.

"In cases of cerebral excitability, or in hyperæsthesia, the bromide is very valuable. In the irritability of young children, or of a preternaturally sensitive nervous system, its action is very marked. In nightmare it is good, associated as it is with gastric disturbance. In those persons who do not bear tonics well, as in those with whom quinine disagrees, producing headache, throbbing, and general discomfort, bromide of potassium given alone with it will produce different effects, and enable quinine to be taken with benefit and comfort. In like manner it acts upon those who cannot take iron without headache, etc. The addition of the bromide to the chalybeate will usually make a marked difference. In convalescence from conditions of debility, where a state of cerebral anæmia with intolerance of ferruginous tonics lingers, the addition of bromide to the steel mixture at once removes the intolerance.

"In these different neurotic agents, each possessing more or less special properties, we have remedies which are of great service in the production of a lessened activity in various parts of the nervous system; and which can be beneficially administered, alone or combined, in a great variety of conditions.

"There is another form of activity which is controlled by neurotic agents, and that is secretion. As regards our present state of knowledge on the subject, no distinct hypotheses can be formed about some of the most marked instances. As regards the use of opium in diarrhœa, we can quite understand its effects from its action upon the nerves of the intestinal canal; by arresting the peristaltic action, the contents of the upper intestines are not so swiftly swept away, while the amount of secretion is at the same time checked. This is all intelligible enough; at the same time the effect of opium, in arresting the activity of the liver and kidneys—in all probability by its effect upon their special ganglia—becomes comprehensible in the lessened formation of urea in baruria, though possibly impaired digestion may be a factor. More special observations have been made, and it is found that, after a full dose of opium, irritation of the lingual nerve does not excite secretion in the submaxillary gland so freely as when opium has not been previously administered. If the narcosis be deep, stronger currents are required to excite secretion, and the quantity of fluid secreted is less. Opium seems to check activity in most secreting organs, except the sudoriparous glands of the skin. The antagonism of opium and belladonna in their action is well seen in their different effects upon the skin. Opium produces free perspiration, while belladonna is very useful for the opposite effect of arresting profuse perspiration. For this purpose, atropia has been resorted to successfully in relieving the night sweats even of phthisical patients. Belladonna, too, checks the activity of the mammary glands, and arrests the flow of milk. It also acts upon the salivary glands, and retards their activity. This, Schiff and Heidenhain think, is achieved by the effect of belladonna in paralyzing the terminal branches of the chorda tympani.

"There is no doubt whatever that neurotics can exercise a pronounced effect over secretion, and that, when added to astringents, opium aids their efficiency very decidedly. Secretion is an action over which nerves exercise control, and, consequently, it is more or less influenced by neurotic agents."